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The discovery of enzymatic photoreactivation and the question of priority: The letters of Salvador Luria and Albert Kelner

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Abstract — Enzymatic photoreactivation of DNA occupies a special place in the history of the DNA repair field. It is indeed the first time that the reversion of alterations in the DNA chemistry leading to lethality was demonstrated. It was soon after shown that this correction is mediated by a specific enzymatic process. A controversy accompanied the events surrounding the 'independent'discovery of this phenomenon by A. Kelner and R. Dulbecco. The exchange of letters with S. Luria illustrates the graceful conciliation role played by him in defining appropriate credit. © Société française de biochimie et biologie moléculaire / Elsevier, Paris

history of science / DNA repair / photoreactivation / ultraviolet radiation / Albert Kelner / Salvador Luria

"If the science of medicine is not to be lowered to the rank of a mere mechanical profession it must preoccupy itself with its history. The pursuit of the development of the human mind, this is the role of the historian."

Maximilien-Paul-Emile Littré
French lexicographer and philosopher

Enzymatic photoreactivation is a repair process during which altered bases in DNA exposed to ultraviolet (UV) radiation are restored to their normal chemistry and conformation [1–3]. Enzymatic photoreactivation is catalyzed by a class of enzymes called DNA photolyases, which operate on covalently bonded dipyrimidines of both the cyclobutyl and the 6-4 varieties [1–3]. All DNA photolyases catalyze the monomerization of dipyrimidines by photochemical reactions which depend on the presence of visible light as a specific cofactor [1–3]. The topic of enzymatic photoreactivation has been shrouded in considerable controversy. The process was discovered in bacteria and was soon shown to operate in multiple prokaryotes and eukaryotes, including vertebrates, to the level of marsupials [1]. For many years the question as to whether or not the photoreactivation of cyclobutane pyrimidine dimers transpires in mammalian cells has been vigorously debated. Several recent publications suggest that photoreactivation of both pyrimidine dimers and 6-4 photoproducts may indeed operate in such cells [4, 5]. The nature of the specific chromophores, the molecules that absorb wavelengths of light that are indispensable to the chemistry of the reactions, was also a subject of confusion for a number of years [1].

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The topic of this essay concerns a lesser known controversy which accompanied the events surrounding the discovery of the phenomenon of enzymatic photoreactivation. Enzymatic photoreactivation of DNA occupies a special place in the history of the evolution and progress of the DNA repair field. The repair of damaged DNA, by which alterations in the chemistry and/or structure of DNA are specifically corrected by one or more biochemical processes, was anticipated soon after the demonstration of the mutagenic effects of ionizing radiation by Hermann J. Muller in 1927 [6] and of UV radiation by Edgar Altenburg in 1934 [7]. However, direct experimental evidence in support of DNA repair did not transpire until Albert Kelner's famous serendipitous discovery, published in 1949 under the title "Effect of visible light on the recovery of *Streptomyces griseus* conidia from ultraviolet irradiation injury", [8] and soon thereafter Renato Dulbecco's independent publication entitled "Reactivation of ultra-violet-inactivated bacteriophage by visible light" [9].

Since both of these publications preceded our understanding that the molecular basis of mutagenesis is rooted in alterations in DNA, or indeed that DNA is the genetic material of cells, neither addressed the phenomenon of DNA repair directly. Kelner came close in commenting that:

> "While it is premature to do more than speculate on the mechanism involved in light-induced recovery, the following is suggested as a working hypothesis. *Much of the killing effect of ultraviolet-light is due to a light-labile alteration of some constituent in the cell. Exposure to visible light restores this altered constituent to its former state.*" [my italics] [8].

Precisely what was the controversy concerning the discovery of photoreactivation? Attentive reading of the paper published by Renato Dulbecco [9] just a few months after that of Kelner [8] reveals the following unusual (for a scientific article) statement.

> "The occurrence of photo-reactivation of ultra-violet irradiated phage was noticed accidentally a few weeks after receiving a personal communication from Dr. A. Kelner that he had discovered recovery of ultra-violet treated spores of Actinomyces upon exposure to visible light."

The events that culminated in this explicit deference of priority are extraordinarily interesting. While researching some of the history of the DNA repair field for a book entitled *"Correcting The Blueprint Of Life. An Historical Account Of The Discovery Of DNA Repair Mechanisms"* [10], I encountered the historian's proverbial dream; the complete original correspondence between Albert Kelner, then a research fellow at the Cold Spring Harbor Laboratory on Long Island, New York, USA, under the mentorship of Milislav Demerec, Director of the Laboratory, and Salvador Luria, then Professor of Genetics at the University of Indiana, in Bloomington, Indiana, USA. The correspondence illuminates the story as clearly and as explicitly as the script for a screenplay. All that is required is to briefly set the stage.

Kelner joined the Cold Spring Harbor Laboratory in 1946 at Demerec's invitation. The discovery of penicillin by Alexander Fleming in 1929, and the subsequent promotion of this discovery by the noted English pathologist W.H. Florey in the late 1930s, stimulated a widespread interest in the phenomenon of antibiosis, especially in the pharmaceutical industry. Demerec, with financial support from the industry, was interested in determining whether bacteria such as *E. coli*, which did not normally produce antibiotics, could be stimulated to do so when mutagenized. He suggested that Kelner expose *E. coli* cells to ionizing radiation and screen mutants for antibiotic production. Since the nearest source of ionizing radiation was in New York City, a considerable distance from Cold Spring Harbor, Kelner decided to explore the more convenient use of UV radiation as a mutagenic agent. He soon became involved (one might more accurately state obsessed), with the desire to understand the reasons for vexing variations in the quantitative survival of *E. coli* cells exposed to UV light in his hands. Despite Demerec's increasing disenchantment with Kelner's dogged fixation on this single experimental nuance, which was clearly tangential to the main question at hand, Kelner dug deeper and deeper into this mystery, eventually becoming convinced that the variations he was observing held significant clues to some sort of biological phenomenon associated with the recovery of cells from the effects of UV radiation. In a long and detailed letter (another historical jewel) that he wrote to Stan Rupert many years later, in which he recounted the events of those days at Cold Spring Harbor, Kelner stated that he was shocked by the devastating results of the atomic bomb explosions that ended the war with the Japanese, and that he was strongly motivated by a humanitarian dream to find a way of curing cells from the damaging effects of ionizing radiation. He secretly hoped that the mechanism of the recovery of cells from UV radiation might operate for all types of radiation.

For a long time Kelner believed that the key variable in his experimental fluctuations was related to the post-irradiation temperature. But a systematic exploration of this variable failed to provide coherent results. Ultimately in 1948, he found the solution to his problems. Sometimes the agar plates spread with irradiated *E. coli* cells were directly exposed to sunlight filtering through the windows of the Jones Laboratory at Cold Spring Harbor for varying periods of time, and sometimes they were not. The extent and amount of exposure to sunlight seemed to correlate with the post-UV radiation recovery and eventually led him to test this directly in controlled experiments. The results of these experiments were immediate and immensely gratifying. Cells exposed to visible light after UV radiation sustained massive recovery of viability.

Unfortunately for the young Kelner, by the time he had unraveled this experimental problem he had exhausted Demerec's patience and had been served notice to leave Cold Spring Harbor by the spring of 1949. Surfacing from the complexities of light-dependent reactivation of UV-inactivation of *E. coli* and spores of the fungus *Streptomyces griseus*, Kelner focused his renewed energy on seeking new employment to support himself and his family. He turned for advice and counsel to Salvador Luria, by then a prominent national figure in microbiology, whom he knew well from Luria's summer visits to Cold Spring Harbor. Indeed, during one of these visits in the summer of 1948, Kelner had discussed his confusing data on what he then believed to be the temperature-dependent recovery of UV-irradiated cells with Luria and Luria's young graduate student Jim Watson.

Here then is Kelner's letter to Luria and the rest of the immediately ensuing correspondence between them. I have also taken the liberty of reproducing verbatim my original editorial comments on specific aspects of this correspondence from *"Correcting The Blueprint Of Life"*.

October 30, 1948

Dear Dr. Luria,

> As a veteran father, I can understand the very full life you and Zella [Luria's wife] must be leading since the arrival of the baby. I hope you and your family are thriving.
>
> There has been a rather exciting development in the research on recovery after irradiation, about which I talked to you last summer. I thought you might be interested in hearing about it, and I would appreciate

your comments. Last summer I had been investigating the temperature-recovery relationship, and found that there was several hundred-fold to a thousand-fold recovery when the *actinomycete* spores were stored in saline at about 15 °C, and at 45 °C, with no or little recovery at 0 and 25–37 °C, the latter being about the optimum temperature range for growth of the organisms. The recovery-temperature curve thus had two peaks.

I have discovered however, another factor which entirely overshadows in importance the temperature effect. This is irradiation of the ultraviolet-treated cells with nothing more than visible light. Under suitable conditions such irradiation will cause over 200 000-fold recovery, such a tremendous recovery that I feel that I have hit upon the key factor within the cell which can bring about recovery after ultraviolet (or X-ray?) treatment. This factor was investigated because I had noticed that suspensions stored on the laboratory shelf in the presence of diffused light from the window had a far greater recovery than suspensions stored in a water bath (at approximately room temperature) which was partially shielded from light. Also because when I moved over to Jones toward the end of the summer, recovery of suspensions in the 35° water bath became high and variable. This turned out to be because the water bath had been placed in front of a window.

My plans are to (1) standardize conditions under which maximum and most rapid recovery will occur, so that I have something to work with, (2) determine whether the light is affecting something within the cells, or something in the menstruum (perhaps peroxides?), (3) investigate the effect of various wave lengths, in order perhaps to get a spectrum of the relative efficacy of various wave lengths on recovery. This may give me a clue as to what compound in the cell is being affected, (4) determine the generality of the phenomenon by studying recovery under standardized conditions of several actinomycetes, fungi, bacteria, and phage.

What do you think of all this?

Conditions for me are in as chaotic a state as ever. Demerec agreed to allow me to stay for this winter so that I could find some sort of job, but he wanted me to work on some problem he had gotten a grant for Vernon [Bryson] for (quite complicated isn't it?) work on resistance of acid-fasts to streptomycin. Had I agreed to work on this problem I could have stayed another year, but I bargained with him to the effect that if he let me work on the recovery problem, I would guarantee not to stay longer than May-until May because there was just enough money left from the Schenley grant to keep me until then. He agreed with a lot of scowls and frowns, and so I have this winter to look for a job, and work on this problem. There is no assistant however, or money for equipment, and so I have become an expert contriver of apparatus made of rubber bands, cardboard and Scotch tape!

The papers on the *actinomyces* mutants, and antibiotic work are all in press; the main one will appear in the January issue of the J. Bacteriology.

I have become quite disheartened about the prospect for a good job, and am about ready to throw up the sponge, and go into some commercial laboratory. I did have some correspondence with Topping of the National Institutes of Health about the possibilities there. But nothing seems to be coming of it. Do you know anyone at the National Institutes of Health who might be interested in the sort of research I have been doing?

I had been hoping that if nothing more I could go down there as a guest investigator for a few weeks this fall, to do the spectrum phase of the research, a phase for which the equipment here is hopelessly inadequate. That would give me a chance to breathe the atmosphere of another laboratory for a change as well as a chance to get an important phase of the work done. If I don't succeed in accomplishing this at NIH, I'll try one of the laboratories in New York. Incidentally, in some of the applications I've been making I took the liberty of giving your name as a character reference. Hope this is all right.

Your comments will be much appreciated.

Sincerely yours
Albert Kelner

There is every indication that Kelner liked and respected Luria well. He apparently viewed Luria very much as a mentor and he openly solicited his advice on the recovery findings (the full details of which are clearly revealed) and he relied heavily on Luria's good graces and considerable reputation in helping him secure employment. Imagine Kelner's shock and surprise when he received the following reply from Luria almost a month later.

November 26, 1948
Dear Kelner,

You will be interested in knowing that Dulbecco has discovered, quite by accident, a phenomenon which may be the counterpart on phage of your discovery on bacteria-ultraviolet inactivated phage is reactivated by visible light at a terrific rate-the conditions are extremely peculiar, and it will take several weeks to know where the radiation acts-Dulbecco has isolated pretty well the active from the inactive bands of light. For the time being it is not clear whether the action is on phage itself, on medium, or on bacteria. We shall keep you informed of any progress, and at the same time I'd like you to let me know if you have some result or idea that may help us. In about 2–3 weeks we ought to have enough data to give you a quantitative summary.

I have made some inquiries concerning positions suitable for you. Would you mind sending me a brief biography (8–10 lines) and list of publications. It may help.

Best regards, also to Mrs. Kelner.

Yours
Luria

P.S. Danny is doing fine, passed the 12 lbs mark, doubling birth weight in 11 weeks.

Kelner immediately shared this letter with Demerec and others at Cold Spring Harbor. In his correspondence to Rupert thirteen years later he commented that "Demerec and the staff at Cold Spring Harbor, especially Barbara McClintock and Caspari were far more indignant and skeptical than I, and told me so. All the letters I wrote (after the first) to Luria were approved by Demerec. Actually I have the highest respect for Luria and Dulbecco and was glad to follow Tom Anderson's advice that the best thing to do about such a matter is to forget it. But after all these years it is proper to let someone else besides myself know what went on. For I believe that it has plagued my career ever since. Of course photoreactivation would have been discovered eventually (Professor Magni, Institute di Genetica, University of Pavia told me last year (in 1960) he was observing it in yeast when my paper was published), by somebody. And even maybe Dulbecco would have. But he certainly knew about my work before making his observation. You can imagine how I must have felt at the time, with no job, or opportunity to work, and anxiety about the future."

But Kelner did not 'forget it'. Urged by Demerec he began writing up his results for publication in the Proceedings of the National Academy of Sciences, of which Demerec was a member, thereby enjoying the privilege of rapid communication to the journal. Perhaps primarily because he was busy with this writing, perhaps for other reasons, the specifics of which we shall never know, Kelner did not immediately respond to Luria's letter of November 26, a nuance of some significance, as we shall presently see. But his concern and unhappiness about this situation were heightened by a second letter from Luria written just prior to Christmas of 1948.

December 23, 1948

Dear Kelner,

Because of the extreme interest that the photoreactivation (it would appear that Luria had already named this phenomenon) of phage will have for virologists, we have thought that Dulbecco should send a note to *Nature* briefly relating the facts. I thought that unless you have already published your observations on bacterial resuscitation, you might like to send in a similar note. I am enclosing a copy of Dulbecco's note.

Dulbecco ran into photoreactivation in a most queer way, by forgetting to put off the fluorescent light on a table on which he had left a pile of plates with irradiated phage to incubate them at room temperature. Next day the top plate had 100 × more plaques than the bottom one, and the intermediate ones had gradually different numbers. He has investigated the phenomenon very thoroughly from a physical point of view, isolating the effective wave-lengths, etc. It is a most exciting thing, and I imagine that the bacterial phenomenon you discovered must also be such.

Please let me know how your plans are developing. There are chances that something suitable for your needs and interest comes to my attention soon, in which case I shall let you know.

With best regards and wishes for the holidays, I am

Yours,
S. E. Luria.

Unfortunately Al Kelner died during the summer of 1994 and I was not able to fully get a first hand measure of this apparently gentle and rather private man, nor to establish precisely what he thought and how he felt during the period between late December 1948 and January 15, 1949, when he replied to Luria's two epistles. When he finally did so he composed a masterpiece of professional sobriety and decorum in which he deliberately adopted a calm, reasoned and forthright appeal to what was obviously a delicate and (at least for him), emotionally charged situation. As mentioned earlier, several people who recall that time, most notably his wife Adelyn, told me that securing Luria's good graces to help find a job was not a trivial motive in his demeanor. Yet he was clearly unwilling to capitulate on the important principle at stake for him: recognition and priority for his years of individual labor. As you shall see, gratifyingly for all concerned this appeal struck a responsive chord in a presumably more than slightly embarrassed and somewhat chastened Luria.

January 15, 1949

Dear Luria,

I want to thank you and Dulbecco for sending a copy of the ms. It was indeed very gratifying to learn that light-induced recovery occurs also in phage, as I had suspected. (You will remember that in my letter of October 30 I mentioned that I planned to try my recovery experiments with phage, but of course that won't be necessary now.) Phage photoreactivation also makes more certain than ever that my feeling that the phenomenon is a general one is correct. There is nothing I should like better than to exchange information with you and Dulbecco; I intend to do so, and hope that we will both progress the faster for it.

However I want to first explain to you as frankly as I can some of my more personal reactions to your letters. And before beginning I know you will agree, that if our positions were reversed you would most certainly feel exactly the same as I do now. It is this: it seemed a most unusual, and almost impossible-to-believe coincidence that Dulbecco's discovery should have entirely independently been made precisely 3–4 weeks after I had written you the essentials of my findings. I do not imply the first impetus to Dulbecco's discovery (the pile of queer plates) was not wholly unplanned; but that my data certainly must have helped in the interpretation, in the exclusion of other possibilities, etc., etc. I remember from last summer how closely you two work together. Now light-induced recovery is certainly not an obvious phenomenon, for if it were then Hollaender, Latarjet, you or Dulbecco

would have discovered it long ago. I'm sure plates have been exposed to light before. Nor does the phenomenon proceed obviously from the Hollaender-Kaufmann infra-red studies; those dealt with mutations and you know yourself the other fundamental differences between their work and ours.

I cannot help feeling-and again I say that if our positions were reversed I am positive you would feel the same way-that my findings had influenced the discovery of phage photoreactivation, and I would have felt much better if my original discovery and its relation to Dulbecco's were mentioned in your ms. to *Nature* and in your discussions with others (such as Anderson, etc.).

What I am confident of is that in the excitement of Dulbecco's discovery, the influence of my findings may have been entirely unconscious and indirect.

I am sure this matter of which I have spoken so frankly will iron itself out, and we can discuss matters in a most friendly manner. Incidentally, Demerec has been exceedingly enthusiastic, helpful and sympathetic to me in this entire matter-both in its scientific and non-scientific or personal aspects.

My best regards to Zella and the new baby, and a happy and scientifically progressive New Year!

Yours,
Albert Kelner.

One cannot fail to be impressed by the apparent efficiency of the US mail service between Cold Spring Harbor, New York and Bloomington, Indiana in those days prior to the technological wonders of facsimile machines and electronic mail. Just 2 days later, on January 17, 1949, Luria received the letter from Kelner quoted above and immediately drafted a detailed response which, in contrast to his earlier correspondence, he formally copied to his graduate student Renato Dulbecco.

January, 17, 1949

Dear Kelner,

I received this morning your letter of January 15. At first I was surprised at your reaction, but I must say that on second reading I saw your point of view and agreed with it. Dulbecco's observations came out in such an astonishingly independent way that the possible subconscious connection between your results and his observation never quite materialized in our minds as one of cause to effect. It must be recognized, however, that an influence of your original communication in formalizing the interpretation may well have occurred. I want to give you the full details of what happened, and then suggest a solution that may be satisfactory to you and Dulbecco both.

1. For several months, we had been puzzled by a lack of reproducibility of plaque counts in pairs of plates used in assaying the titer of irradiated phages. Tests of several kinds failed to give any explanation, and the observation was shelved as a nuisance. This was in September (1948). The reception of your letter failed to suggest to me the obvious interpretation, that one of the two plates sometimes remained on top of the other on the table for an hour or more, and therefore received more light. Incidentally, this difference between assay plates only came up either in Cold Spring Harbor, with lots of diffused light, or after we installed here fluorescent lights directly on the lab tables. As a matter of fact, regular incandescent bulbs give out very little of the photoreactivating wave-lengths.

2. While I was in New Haven November 10–18 Dulbecco was doing experiments on the effect of temperature on reactivation by multiple infection. In a series at room temperature (26°), at 33° and at 37° it came out that there was an excess of reactivation at 26°. In a second experiment (20° and 37°) there was an excess at room temperature again. He did a third experiment, comparing 26° incubator room and regular room, and in the latter one there was an excess. In thinking of possible differences he noticed that the plate that was on top of the pile at room temperature had the most plaques, and the lower ones had decreasing numbers. The pile of plates had been under the fluorescent light for several hours. At this point he remembered the difference between plates in pairs and tested for it. By the time he met me in Chicago (November 19) at a oint seminar with Szilard he had explained the difference.

3. Your letter (of October 30, 1948) arrived around November 1. I told Dulbecco about it, but he did not read the letter. We did at no time plan to test photoreactivation on phage. *A posteriori* and incidentally, the simplest test for phage reactivation would have failed, since phage is only reactivated in [the] presence of bacteria. I am perfectly sure that Dulbecco had no conscious recollection of your results, since I remember that I reminded him of them in Chicago. I think, however, [it] very possible that the process of interpretation was accelerated from having heard of your results a few weeks earlier. That he did not think of them consciously can easily be seen from his protocol of daily experiments, in which you can see that he was groping completely in the dark.

At this point in his letter Luria offered a remarkable gesture of capitulation in restoring priority for the discovery of photoreactivation to his younger colleague, and simultaneously extending a candid apology for his previous failure to acknowledge the obvious importance that Kelner attributed to his experimental findings. The letter continues.

4. In view of the above, I think it is only fair that you should have the complete credit for the first discovery of photoreactivation. My suggestions, which I want to submit to you for approval before anything is done

(besides stopping publication of the note in *Nature*, which I have already done telegraphically), are the following:

a) Dulbecco's note could have the following paragraph inserted after the first one:

'The occurrence of photoreactivation of ultraviolet irradiated phage was noticed accidentally a few weeks after receiving a personal communication from Dr. A. Kelner that he had discovered recovery of ultraviolet treated spores of actinomyces upon exposure to visible light. My observation indicated the correctness of Dr. Kelner's suggestion that the phenomenon discovered by him may be of general occurrence for a number of biological objects.'

Also, in the first paragraph, the word 'discovered ' on line 4 could be replaced by 'observed'.

b) If you consider this satisfactory, the note on phage could be sent on to publication, if you do not expect to publish your discovery soon. It is important to us to make the distinction of photoreactivation from reactivation by multiple infection known soon, since it may affect the mechanism of the latter reactivation, on which there are several papers in press. If, however, you plan to publish soon, Dulbecco agrees to delay publication of his observation until that time. Incidentally, we would appreciate your giving him permission to do so as soon as possible; most of his data, as you will realize have more relevance for phagology than for the mechanisms of photoreactivation, and that is what we are mainly interested in.

After all this on a technical level, let me personally assure you that we never had the slightest intention to capture priority from you, as our prompt willingness to abide by your decision proves it. You can imagine that we were very much upset by the possible consequences of photoreactivation of phage for the whole problem of the genetic interpretation of reactivation by multiple infection (and we still are in part). When Szilard and then Delbrück suggested that the thing should be announced quickly to keep other people from misinterpreting results, we did so, and at that time I wrote to you for your opinion. After failing to hear from you, I sent the note to *Nature*, without giving enough thought to the possible influence that your discovery may have had on the course of Dulbecco's work. As I already stated before, there was no conscious influence, and the possible subconscious one I failed to appreciate sufficiently.

I hope that my suggestions meet with your approval. Please do not let this apparent misunderstanding alter your good feelings toward us. If you had written me immediately there would have been no such complication.

With best regards, also from Dulbecco. I remain,

Yours sincerely,

S. E. Luria.
cc. R. Dulbecco

Luria's comment about failing to obtain a response from Kelner to his letter of November 26, 1948 is significant. As he pointed out, having specifically informed Kelner about the observations in his own laboratory, he (Luria) was focused on the imperative of forging ahead with a communication to *Nature*, an imperative that was apparently reinforced by his discussions with Max Delbrück and Leo Szilard. The rationale for this haste is amply documented in the first paragraph of the paper that was eventually published by Dulbecco in *Nature*.

> Since [the] phenomenon [of photoreactivation] may cause serious misinterpretation of results obtained in working with irradiated phage, it may be useful to report it at this early stage of its investigation" (Dulbecco, R. 1949. *Nature* 163, 949–950.]

It is evident from Luria's January 17, 1949 letter to Kelner as well as from the perspective adopted by Dulbecco in his *Nature* paper, that Luria was not especially interested in the recovery by phage or bacteria from the inactivating effects of UV radiation, even though in his earlier letter written just prior to Xmas of 1948 he described Dulbecco's result as 'a most exciting thing'. At that stage of his career Luria's focal point of research was the phenomenon of multiplicity reactivation of UV-irradiated phage, a phenomenon that he hoped might provide insights into the mechanism of phage replication in bacteria. Indeed, neither the episode of his extensive correspondence with Kelner, nor Dulbecco's independent discovery of photoreactivation were recounted in his autobiography '*A Slot Machine, A Broken Test Tube*.' And Dulbecco's *Nature* paper was published without Luria as a co-author.

To close this chapter of the photoreactivation story here is Kelner's response to Luria's gracious letter of conciliation and apology.

January, 20, 1949

Dear Luria,

The solution you suggest is a most fair and decent one, and if the insertion and emendation you suggest are included in the note to *Nature* I of course give my whole-hearted approval for the immediate publication of Dulbecco's findings.

At Demerec's suggestion I had submitted a manuscript for publication some weeks ago, and perhaps if possible you might also want to mention this paper as 'in press, Proc. Natl. Acad. Sci.' Although this is not too important a point, and it would not be worth delaying publication of Dulbecco's ms. to include this reference.

This is a hasty letter for I wanted to write immediately to go ahead with publication of the note to *Nature*. I'll send a longer letter soon, with a copy of my manuscript. I'm very glad to have this affair off my mind and look forward to discussing the scientific points of this phenomenon.

I agree that photoreactivation is an important discovery for phagology. Indeed one reason I have not

discussed the phenomenon with very many people is that I wanted to give your laboratory a chance to work out the problem and announce your findings as they relate to reactivation in general yourselves.

With best wishes, and thanking you and Dulbecco for your honest and sincere reaction to my letters.

I am

Sincerely yours,
Albert Kelner.

Since the publication of *"Correcting The Blueprint Of Life"*, a number of readers have commented to me on Luria's extraordinary grace in accommodating his younger colleague in the manner in which he did, and more than a few have remarked on how much the gestalt of scientific collegiality has changed in the past 50 years!

Kelner and Dulbecco are appropriately credited with the discovery of photoreactivation. However, not unexpectedly, the formal comprehension of this process as a discrete biochemical pathway for the repair of photoproducts in DNA did not transpire until the DNA molecule itself came to occupy its recognized role as the chemical basis of heredity. Not long after this seminal discovery was announced by Watson and Crick in 1953, Stan Rupert together with Sol Goodgal at Johns Hopkins University went in search of the enzyme that catalyzes photoreactivation and found it, both in *E. coli* and in yeast in 1956. In 1974, on the occasion of the 21st anniversary of his and Jim Watson's historic publication in *Nature* announcing their model of their structure of DNA Francis Crick wrote:

"We totally missed the possible role of enzymes in repair, although, due to Claud Rupert's early very elegant work on photoreactivation, I later came to realize that DNA is so precious that probably many distinct repair mechanisms would exist. Nowadays one could hardly discuss mutation without considering repair at the same time." [11].

Acknowledgments

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References

[1] Friedberg E.C., Walker G.C., Siede W., DNA Repair and Mutagenesis, ASM Press, Washington D.C., 1995, 698 p.

[2] Sancar A., Structure and function of photolyase, Biochemistry 33 (1994) 2–9.

[3] Todo T. et al., A new photoreactivating enzyme that specifically repairs ultraviolet light-induced (6-4) photoproducts, Nature 361 (1993) 371–374.

[4] Sutherland B.M., Bennett P.V., Human white blood cells contain cyclobutyl pyrimidine dimer photolyase, Proc. Natl. Acad. Sci. USA 92 (1995) 9732–9736.

[5] Todo T., Tsuji H., Otoshi E., Hitomi K., Kim S.T., Ikenaga M., Characterization of a human homolog of (6-4) photolyase, Mutat. Res. 384 (1997) 195–204.

[6] Muller H.J., Artificial transmutation of the gene, Science 66 (1927) 84–87.

[7] Altenburg E., The artificial production of mutations of ultraviolet light, Am. Nat. 68 (1934) 491–507.

[8] Kelner A., Effect of visible light on the recovery of *Streptomyces griseus* conidia from ultraviolet irradiation, Proc. Natl. Acad. Sci. USA 35 (1949) 73–79.

[9] Dulbecco R., Reactivation of ultra-violet-inactivated bacteriophage by visible light, Nature 163 (1949) 949–950.

[10] Friedberg E.C., Correcting the Blueprint of Life. An Historical Account of the Discovery of DNA Repair Mechanisms, Cold Spring Harbor Laboratory Press, 1997, 210 p.

[11] Crick F.H.C., The double helix, a personal view, Nature 248 (1974) 766–769.